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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,534	01/25/2002	Harry R. Davis	CV01378K	2339

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER

WANG, SHENGJUN

ART UNIT PAPER NUMBER

1617

DATE MAILED: 05/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/057,534	Applicant(s) DAVIS ET AL.	
	Examiner Shengjun Wang	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-81 is/are pending in the application.
- 4a) Of the above claim(s) 4,29,30,37-69,73,78 and 81 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-28,31-36,70-72,74-77,79 and 80 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/03/03, 12/01/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted February 17, 2004 is acknowledged.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-3, 5-28, 31-36, 70-72, 74-77 and 79-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rosenblum et al. (US 5,631,365, IDS) in view of Albright (US 5,300,288), Dechow (US 4,837,255), and Davis (US 5,661,145, IDS).

3. Rosenblum et al. teaches that hydroxy-substituted azetidinone compounds, including ezatemibe, are known to be useful for lowering cholesterol level. Rosenblum et al. further teaches that the hydroxy-substituted azetidinone compounds are particularly useful in combination with a cholesterol biosynthesis inhibitor. See, particularly, column 2, line 15 to column 3, line 66, example 6 in column 31-33.

4. Rosenblum et al. does not teach expressly a combination of a hydroxy-substituted azetidinone compounds, e.g., ezatemibe, and a bile acid sequestrant, e.g., cholestyramine, or further with a cholesterol biosynthesis inhibitor, e.g., simvastatin.

5. However, as shown in Albright, cholestyramine is an old and well-known cholesterol-lowering agent. See, column 2, lines 3-7. Dechow particularly, teaches a method of lowering cholesterol by administering to a patient a composition comprising cholestyramine. See,

Art Unit: 1617

particularly, the claims. Davis teaches that simvastatin is a known cholesterol biosynthesis inhibitor, and is particularly useful with lactam cholesterol absorption inhibitor. See, particularly, column 2, lines 51-63.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to make cholesterol lowering composition comprising the hydroxy-substituted azetidinone compound, ezatemibe, and the well-known cholesterol lowering agent, cholestyramine.

A person of ordinary skill in the art would have been motivated to make cholesterol lowering composition comprising the hydroxy-substituted azetidinone compound, ezatemibe, and the well-known cholesterol lowering agent, cholestyramine. It is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, the claimed invention which is a combination of two known cholesterol lowering agent sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069. The further employment of simvastatin in the combination is obvious because the hydroxy-substituted azetidinone compounds are known to be useful with cholesterol biosynthesis inhibitor. Further, the optimization of a result effective parameter, e.g., effective amount of a therapeutical agent, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215.

Response to the Arguments

Applicants' amendments and remarks submitted February 17, 2004 have been fully considered, but are not persuasive for reasons discussed below.

Art Unit: 1617

6. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the teaching, suggestion and motivation are found both in the cited references and in the knowledge generally available to one of ordinary skill in the art. Particularly, each of the active ingredients in the claimed combination therapy are known to be useful for the same therapeutical purpose, the combination would have been obvious to one of ordinary skill in the art. Further, cited references teach to use combination of therapeutic agents with different biochemical functions.

7. Applicants contend that examiner's citation of *In re Kerkhoven* is improper for instant situation because the agents in the combination have different biological functions. The examiner disagrees. Even the agents herein have different biological functions, the ultimate utility are the same, i.e., lowering cholesterol. For the purpose of lowering cholesterol, the combination would have been obvious. Further, cited references teach to use combination of therapeutic agents with different biochemical functions, one of ordinary skill in the art would have been further motivated to combine the agents for their difference in biological functions.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1617

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang, Ph.D. whose telephone number is (571)272-0632. The examiner can normally be reached on Monday-Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9302.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

SHENGJUN WANG
PRIMARY EXAMINER



Shengjun Wang

May 8, 2004